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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/538,514	06/09/2005	Tsuyoshi Naganuma	Q88061	1878

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EXAMINER	
WEBB, WALTER E	
ART UNIT	PAPER NUMBER
1612	
MAIL DATE	DELIVERY MODE
10/08/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/538,514	NAGANUMA ET AL.	
	Examiner	Art Unit	
	WALTER E. WEBB	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8,9,11,12,27 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 8, 9, 11, 12, 27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/22/2009 has been entered.

Applicants' arguments, filed 7/22/2009, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103--previous

Claims 1, 8, 9, 11, 12 and 27 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Kitazawa et al., (US 5,387,603) in view of Ishihara et al., (US 2002/0177593) and in further view of Salpekar et al., (US 4,757,090) and Shah (US 5,370,878). This rejection also applies to newly added **claim 28**.

Kitazawa et al. teach the compound of claim 1 (KMD-3213) (see col. 62, claim 10), and a method of using the compound for the treatment of dysuria (see col. 1, lines 57-59.). They also teach that the compound or the pharmaceutically acceptable salts thereof can be administered orally as tablets and capsules in accordance with conventional molding methods (see col. 16, lines 15-23). In regard to **claim 28**, the reference teaches an acceptable dosage range from about 0.5 to 500 mg per adult human by an oral administration per day (see col. 16, lines 23-25).

Kitazawa et al. does not teach combining the compound with D-mannitol, pregeletinized starch, magnesium stearate, sodium lauryl sulfate, light-shielding, or a dissolution rate for the capsule.

Ishihara et al. teach a method for treating dysuria with agents for further improving excretory potency of the urinary bladder. (See Abstract (57).) Agents include KMD-3213 as well as other compounds (see paragraphs [0559], [0553], [0556], and [0577].) They teach that these agents can be administered in capsule or tablet form further comprising a light-shielding coating agent like titanium oxide, D-mannitol, magnesium stearate, and sodium lauryl sulfate (see paragraphs [0618], [0626], [0620], and [0596]. Pharmaceutical compositons can be produced according to a conventional method in the field, for example, a method described in The Japanese Pharmacopoeia (se paragraph [0619].

The combination of Kitazawa et al., and Ishihara et al., differs from the instant claims insofar as it does not teach a capsule comprising <u>partially</u> pregelatinized starch wherein 85% dissolution time is not more than 15 minutes.

Salpekar et al. teach a composition and a direct tableting process, where pregelatinized starch is included in an amount effective for imparting to the composition a short dissolution time, e.g. about 20 minutes or less for 80% or more of the active compound to dissolve. (See abstract, and col. 2, lines 60-66.) They teach adding compatible mixtures of two or more lubricants such as sodium lauryl sulfate, magnesium stearate at 0.10 to about 1 percent based on the dry weight of the composition. (See col. 3, lines 13-23.) These amounts are such that disintigration, dissolution time will not be increased. (See col. 3, lines 5-10.) Salpekar does not teach a compound formula of claim 1.

Shah also teaches a composition with short dissolution time, but suggests using either partially or completely pregelatinized starch. (See col. 3, lines 56-64.) Shah does not teach a compound formula of claim 1.

Generally, it is also *prima facie* obvious to select a known material based on its suitability for its intended use (see MPEP 2144.06). Also, established precedent holds that it is generally obvious to add known ingredients to known compositions with the expectation of obtaining their known function (see Id). Thus it would have been obvious to use D-mannitol, pregelatinized starch, magnesium stearate, sodium lauryl sulfate, light-shielding to formulate the capsule composition of Kitazawa et al., as evidenced by Ishihara et al, Salpekar et al., and Shah.

The artisan would have been further motivated to use pregelatinized starch for its ability to impart a short dissolution time, e.g. about 20 minutes or less for 80% or more of the active compound to dissolve.

Generally, in the case where the claimed ranges "overlap or lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. See MPEP 2144.05. Since the claimed range for the dissolution, and daily dose of the indoline compound overlaps with the dissolution time of Salpekar et al. for the pregelatinized starch, and the dosage of the indoline compound of Kitazawa et al., a prima facie case of obviousness exists.

Response to Arguments

A declaration under 37 C.F.R 1.132, filed 7/22/2009 by Tsuyoshi Naganuma, was submitted with data to rebut the 103 rejection above. The data describes different formulation methods for several capsules, i.e. Examples 1 and 2, and capsules C, A, B, H, F and M. Dissolution rate (%) after 15 minutes, and encapsulation filling were performed for each capsule. It is apparent from Table 1 at page 10, that variation of components affected the dissolution % and encapsulation filling. Affiant concluded, "It is apparent that the use of magnesium stearate as a lubricant influenced the compositions containing the lubricant to increase their dissolution time" (see pg. 12 of declaration, second paragraph). However, magnesium stearate was used in every example except comparative Capsule A. It is not clear how the mere use of it necessarily increases the dissolution rate when its use in the present invention examples did not lower the dissolution rate. Furthermore, Salpekar et al. teaches combining sodium lauryl sulfate and magnesium stearate in amounts such that disintegration and dissolution time will not be increased. The artisan would thus be

expected to use magnesium stearate in amounts such that the dissolution time would not increase.

Affiant based the formulation of the comparative examples on the prior art references individually. However, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.,* 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). It would have been obvious to use D-mannitol, pregelatinized starch, magnesium stearate and sodium lauryl sulfate to formulate the capsule composition of Kitazawa et al. based on their suitability for their intended use.

Affiant argues that corn starch is worse than partially pregelatinized starch in regard to dissolution rate. However it is not clear why such a comparison is being made, since was no suggestion by the Examiner or the prior art references that corn starch is equivalent to partially pregelatinized starch.

Affiant argues that, since the comparative capsules showed less than 20% dissolution and a lower dissolution rate, it is apparent that the general mention of partially pregelatinized starch in Salpekar does not teach the immediate dissolution property exhibited by the capsules of the present invention. However, Salpekar teaches the use of pregelatinized starch in an amount effective for imparting to the composition a short dissolution time, e.g. about 20 minutes or less for 80% or more of active the compound to dissolve. Therefore, affiant's data showing more than 80% dissolution in less than 20 minutes is not unexpected. Affiant's comparison is also not

justified, since it is clear from Salpekar that the amount of pregelatinized starch depends on the expected result. The artisan would reasonably adjust the amount of the pregelatinized starch such that the dissolution time would match about 20 minutes or less for 80% or more of active compound to dissolve.

Lastly, affiant argues that, based on the results of Capsule M, Ishihara fails to teach or suggest how to achieve immediate dissolution properties and good manufacturing aptitude without causing filling problems during encapsulation. However, Ishihara was used to show that light-shielding coating such as titanium oxide, D-mannitol, magnesium stearate, and sodium lauryl sulfate were known to be useful in formulating a capsule for KMD-3213. The dissolution properties were taught in Salpekar, and the artisan would reasonably expect good manufacturing aptitude without filling problems with the use of these materials.

Affiant does not mention that the results are unexpected, but even if they were, the instant claims are not commensurate in scope. The instant claim 1, for example, is not limited to a specific partially pregelatinized starch, or lubricant. The instant claims also differ from the examples presented insofar as they do not claim use of two types of partially pregelatinized starch. The instant claims also do not specify relative amounts for each component of the composition.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the

grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 8:00am-4:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Walter E. Webb
/Walter E Webb/
Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612